

Ion Composition Elucidation (ICE) of Ions from Trace Levels of Pharmaceuticals and Disinfection Byproducts in Water Supplies

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INTRODUCTION

Good-quality, low resolution mass spectra provide tentative identifications of compounds through comparison to library mass spectra. When no matches or multiple matches are found, "exact masses" of ions measured by peak matching with a mass resolution of 10,000 can provide unique compositions of ions containing C, H, N, O, P, or S atoms with masses up to 150 Da. Using 20,000 resolution, Ion Composition Elucidation (ICE) increases the mass limit of ions for which compositions can be uniquely determined to 600 Da. ICE utilizes Mass Peak Profiling from Selected Ion Recording Data (MPPSIRD) to acquire data and a Profile Generation Model (PGM) for its automated interpretation. ICE is accomplished by measuring the exact masses and relative abundances of mass peak profiles arising from less abundant isotopes of the elements comprising the ions such as ^{13}C , ^{15}N , and ^{34}S (1). Three examples will illustrate the utility of this recently developed analytical approach for identifying trace levels of compounds in complex sample extracts.

MPPSIRD

Selected ion recording (or multiple ion detection) is often used to monitor only the maxima of multiple mass peak profiles for analytes and internal standards in order to increase sensitivity by a factor of 100 relative to full scanning. MPPSIRD consists of monitoring multiple m/z ratios across multiple profiles as a chromatographic peak elutes. In these examples, five m/z ratios were monitored across the top portions of lock and calibration profiles and seven m/z ratios were monitored across the analyte profiles. The areas under the chromatographic peaks were plotted to provide partial mass peak profiles. The weighted average of the top several areas delineating a molecular ion (M) or fragment ion (F) profile provided its exact mass. The ratio of the sum of the profile-delineating areas for profiles arising from ions containing higher isotopes (M+1, M+2, F+1, or F+2 profiles) to the sum of areas for the M or F profile provided the relative abundance of the higher-mass profile (2).

Acetaminophen or Surfynol 104?

Displayed in Figure 1a, 1b, and 1c, respectively, are: the NIST library mass spectrum of acetaminophen ($\text{C}_8\text{H}_9\text{NO}_2$), a commonly used analgesic; a background subtracted mass spectrum from an extract of 100 L of lake water; and the NIST library mass spectrum for Surfynol 104 ($\text{C}_{14}\text{H}_{26}\text{O}_2$), a wetting agent used in household and industrial cleaners. The lake water extract contained hundreds of compounds, some of which degraded the gas chromatography column interfaced to a Finnigan MAT 900S mass spectrometer. Consequently, background subtracted mass spectra often displayed ions not associated with the compound of interest, and numerous, questionable library matches resulted. The presence of either widely used compound in the lake was plausible and both would normally be purchased to compare mass spectra and retention times to those of the analyte. MPPSIRD was used to acquire data with 10,000 resolution to plot the partial profiles in Figure 2. The three exact mass defects and two relative abundances from Figure 2a were entered into the PGM to provide the first two compositions in Table 1 that were possible based on the exact mass of the m/z 151 ion within the error limits of its determination (± 6 ppm for 1 determination with 10,000 resolution). Each "X" indicates disagreement between the experimental and calculated values for a mass defect or relative abundance.

Therefore, the first composition was rejected. Only the second composition, $\text{C}_{10}\text{H}_{15}\text{O}^+$, remained viable for the m/z 151 ion. Therefore, acetaminophen, which yields $\text{C}_8\text{H}_9\text{NO}_2^+$ (m/z 151.06333) as M, was not the analyte. The barely discernable m/z 190 ion in Figure 1b was investigated similarly (Figure 2b and Table 1) and was found to be $\text{C}_{14}\text{H}_{22}^+$ (m/z 190.17201), which would result from the neutral loss of two water molecules (36.02113 Da) from Surfynol 104 (226.19328 - 190.17201 = 36.02127 Da). Clearly, purchase of Surfynol 104 in hope of confirming this identification would be justified. Interferences overwhelmed the m/z 192 ion with a calculated abundance of 1.16% relative to the m/z 190 ion. Interference with the F+2 or M+2 profile is common for extracts containing hundreds of compounds when F or M has such a small abundance in the full mass spectrum.

#	RDB Range	Composition	M	M+1	M+2	F+1 (F+1 Range)	F+2 (F+2 Range)
1	0.0	$\text{C}_8\text{H}_9\text{NO}_2$.11209	.11499	.11686	X	X
2	3.5	$\text{C}_{10}\text{H}_{15}\text{O}$.11229	.11570	.11848	X	X
Experimental Values:		.11225	.11581	.11934	11.98		0.91
m/z = 190.17201 ± 6 ppm							
1	0.5	$\text{C}_{14}\text{H}_{22}$.17195	.17493		X	X
2	4.0	$\text{C}_{14}\text{H}_{24}$.17215	.17556		X	X
Experimental Values:		.17201	.17553		15.67		

Table 1. Possible Compositions Based on Experimental Exact Mass Defects and Relative Abundances for Fragment Ions with m/z 151, 152, 153 and 190, 191, 192.

Phenytol

Six prominent ions appear in both the poor-quality background subtracted mass spectrum in Figure 3a for a compound in the same lake water extract and the NIST library entry for the sedative phenytol in Figure 3b. However, the many additional ions in Figure 3a limited confidence in this match. The partial profiles for the molecular ion of phenytol in Figure 4 were obtained with 25,000 resolution. Even at this resolution, a low-mass interference inflated slightly the %M+1 value, and the M+2 profile was useless. In the top part of Table 2 are listed three compositions that provided calculated mass defects for the M and M+1 partial profiles and a relative abundance for the M+1 partial profile consistent with the measured values. The nine compositions in the lower part of Table 2 were consistent with the measured exact mass of the m/z 180 ion. In Figure 4b, the F+1 and F+2 partial profiles were both dominated by interferences. The neutral loss difference between m/z 252.08992 and m/z 180.08106 is 72.00886 Da and corresponds to $\text{C}_2\text{H}_2\text{NO}_2$ (72.00855 Da). This neutral loss from composition 36 provided composition 9 for the fragment ion. No other M composition contains the two O atoms required to provide the observed neutral loss. Composition 36 is the composition of the molecular ion from phenytol. Clearly, purchase of this standard for probable confirmation of the compound's identity would be justified.

#	RDB Range	Composition	M	M+1	M+2	F+1 (F+1 Range)	F+2 (F+2 Range)
30	3.0	$\text{C}_8\text{H}_9\text{NO}_2$.09057	.09278	.09444	X	X
35	6.0	$\text{C}_{10}\text{H}_{15}\text{O}$.08994	.09248	.09494	X	X
36	11.0	$\text{C}_{14}\text{H}_{22}$.08988	.09324	.09644	X	X
Experimental Values:		.08992	.09296	.09644			
m/z = 180.08106 ± 6 ppm							
1	2.5	$\text{C}_{14}\text{H}_{22}$.08092	.08144	.08196	X	X
2	0.5	$\text{C}_{14}\text{H}_{24}$.08044	.08144	.08196	X	X
3	1.5	$\text{C}_{14}\text{H}_{26}$.08144	.08196	.08248	X	X
4	0.5	$\text{C}_{14}\text{H}_{28}$.08196	.08248	.08299	X	X
5	0.0	$\text{C}_{14}\text{H}_{30}$.08200	.08248	.08299	X	X
6	0.0	$\text{C}_{14}\text{H}_{32}$.08179	.08196	.08212	X	X
7	6.0	$\text{C}_{14}\text{H}_{34}$.08112	.08164	.08212	X	X
8	5.0	$\text{C}_{14}\text{H}_{36}$.08164	.08196	.08212	X	X
9	9.5	$\text{C}_{14}\text{H}_{38}$.08132			X	X

Table 2. Possible Compositions Based on Experimental Exact Mass Defects and Relative Abundances for Ions with m/z 252, 253, 254 and 180, 181, 182.

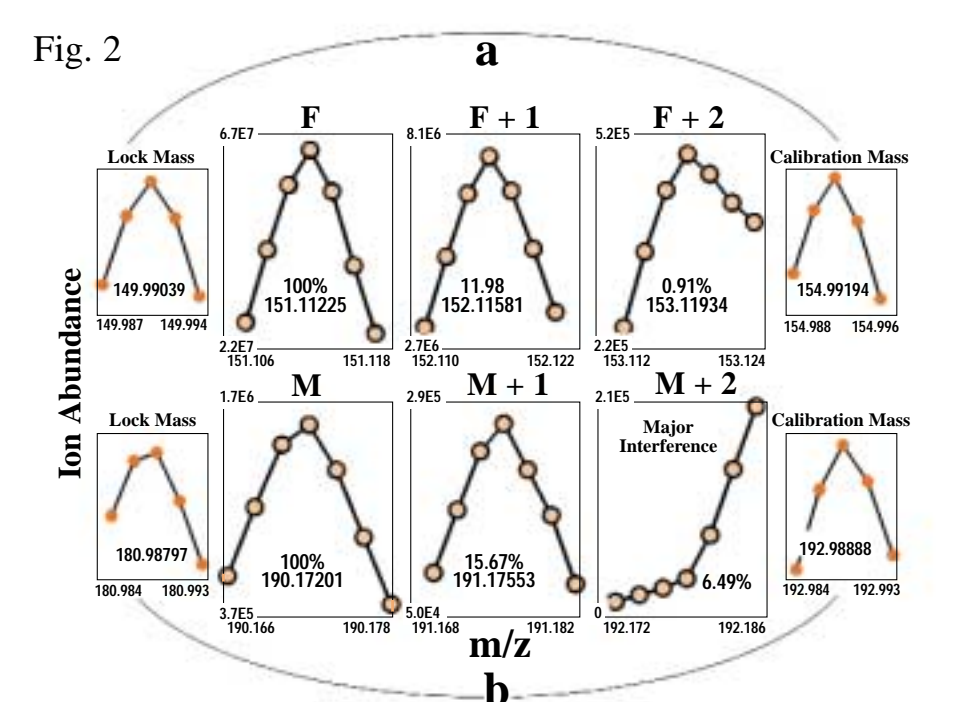
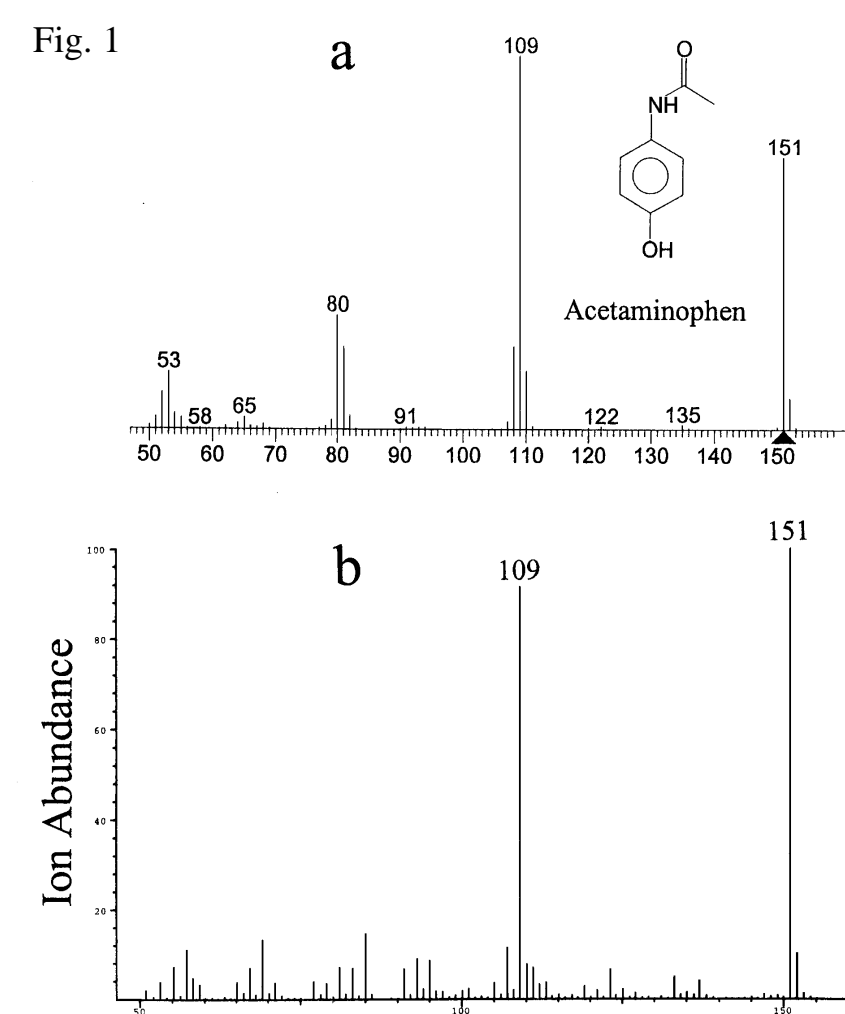


Figure 2. Partial mass peak profiles for (a) m/z 151, 152, and 153 and (b) m/z 190, 191, and 192.

